Health Advisory:

Manufacturer's Recall of Human Rabies Vaccine

April 3, 2004

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SUBJECT: **Manufacturer's Recall of Human Rabies Vaccine**

CDC and the Food and Drug Administration (FDA) have been notified that a recent quality-assurance test of IMOVAX(r) Rabies Vaccine (Aventis Pasteur, Swiftwater, Pennsylvania) identified the presence of noninactivated Pitman-Moore virus (the attenuated vaccine strain) in a single product lot. IMOVAX(r) is an inactivated viral vaccine and should not contain live virus. The vaccine lot containing noninactivated virus was not distributed.

As a precautionary measure, Aventis Pasteur initiated a voluntary recall of lot numbers X0667-2, X0667-3, W1419-2, and W1419-3, which were produced during the same period as the lot that contained noninactivated Pitman-Moore virus. These four lots, which were distributed in the United States from September 23, 2003 through April 2, 2004, passed all FDA-approved release tests, including testing to confirm the absence of live virus. These test results suggest that any potential risk to those vaccinated with recalled vaccine is likely to be low. No unusual adverse events associated with the recalled vaccine have been reported.

The manufacturer has indicated that additional lots of recalled vaccine were distributed internationally. These lots also passed all release tests, including testing to confirm the absence of live virus. The manufacturer is working with regulatory authorities to determine lot numbers of vaccine and countries that might have received recalled lots. More information about these internationally distributed lots will be provided as it becomes available.

Aventis Pasteur is providing additional detailed information to all distributors and providers. Health-care providers should contact persons who received recalled vaccine to implement the recommendations outlined in this notice (see Recommendations for Persons Who Received Recalled Vaccine). In addition, persons who know they received rabies vaccine between September 23, 2003, and April 2, 2004, should contact their health-care providers to determine whether they received vaccine from one of the four lots being recalled and, if so, whether they should

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be treated as outlined below. Vaccine distributors and health-care providers who have any remaining doses of the recalled lots should not use them and should contact Aventis Pasteur regarding their disposition. Information about this recall is available from the Aventis Pasteur Medical Information Services Department, telephone 800-835-3587, or at http://www.vaccineshoppe.com.

All persons who have begun a rabies vaccination series (whether for pre- or postexposure prophylaxis) must complete that vaccination series on time, using nonrecalled vaccine. Information about human rabies prevention based on current recommendations of the Advisory Committee on Immunization Practices (ACIP) is available at http://www.cdc.gov/mmwr/preview/mmwrhtml/00056176.htm.

Recommendations for Persons Who Received Recalled Rabies Vaccine

Most persons receiving rabies vaccine do so because of exposure to a rabid animal, and treatment is needed to prevent fatal illness. Thus, persons who are receiving postexposure prophylaxis (PEP) must not omit or delay receiving any remaining injections; injections needed to complete the series should use nonrecalled vaccine. Recalled vaccine is considered fully immunogenic, and previously administered doses can be considered a dose in a PEP regimen.

Although unlikely, a theoretical possibility exists that persons who received vaccine from a recalled lot could have been exposed to the noninactivated Pitman-Moore vaccine strain of rabies virus. Even in the event of such an exposure, the timely administration of treatment, as described here, will help to ensure negligible risk to persons who have received vaccine from a recalled lot. Persons who received recalled vaccine should receive treatment equivalent to PEP, similar to published guidelines, as follows:

Persons who were vaccinated with recalled vaccine as part of a course of PEP for a possible rabies exposure.

- Not previously immune (i.e., persons who had not received at least 3 doses of vaccine at some time before the possible rabies exposure). Persons without preexisting immunity who have a possible rabies exposure routinely receive a 5-dose postexposure immunization series. If this postexposure series has not already been completed, such persons should complete the full postexposure series, using nonrecalled vaccine to complete the series. Doses that have been administered already as part of the 5-dose series need not be repeated, even if recalled vaccine was used. In addition, if rabies immune globulin (RIG)* was not administered with the first dose of vaccine and it has been <7 days since the first dose of vaccine, RIG should be administered at this time. Once PEP is completed, persons are considered fully vaccinated

against both the original rabies exposure and any possible exposure to noninactivated virus in the recalled vaccine.

- Previously immune (i.e., persons who had received at least 3 doses of vaccine at some time before the possible rabies exposure). Persons with preexisting immunity (i.e., who have completed a full preexposure or postexposure vaccination series) who then have a possible rabies exposure routinely receive 2 booster doses of rabies vaccine. If one or both doses already were administered using recalled vaccine, such persons should receive 2 more doses, using nonrecalled vaccine. RIG is not recommended.

Persons who were vaccinated with recalled vaccine for reasons other than a possible rabies exposure.

- Not previously immune (i.e., persons who had not received at least 3 doses of vaccine at some previous time). Persons without preexisting immunity who received recalled vaccine as part of a 3-dose preexposure vaccination series should receive additional doses using nonrecalled vaccine for a total of 5 doses (dosing intervals should follow the PEP schedule as closely as possible). RIG* is recommended if <7 days have elapsed since administration of the first dose of vaccine.

- Previously immune (i.e., persons who had received at least 3 doses of vaccine at some previous time). Persons with preexisting immunity (i.e., who have completed a full preexposure or postexposure vaccination series before they received recalled vaccine) who received recalled vaccine as a routine booster dose should receive 2 additional doses of nonrecalled vaccine. RIG is not recommended.

All clinically significant adverse events following receipt of rabies vaccine should be reported to 1) Aventis Pasteur, telephone 800-835-3587 and 2) the Vaccine Adverse Event Reporting System (VAERS) at http://www.vaers.org, or telephone 800-822-7967. Additional information about rabies and its prevention is available from CDC, telephone 404-639-1050, or at http://www.cdc.gov/ncidod/dvrd/rabies.

- Where available (including the United States), Human Rabies Immune Globulin (HRIG) is preferred and is administered in a dose of 20 IU/kg. Where HRIG is not available, Equine Rabies Immune Globulin may be used in a dose of 40 IU/kg. These dosages are applicable for all age groups, including children. For persons receiving RIG after having received recalled vaccine administered as part of PEP, as much of the dose as is anatomically feasible should be infiltrated at the site of the original rabies exposure (e.g., a wound), and as much of the remaining dose as is anatomically feasible should be infiltrated at the site(s) where the recalled vaccine was injected. If any RIG remains, it

should be administered intramuscularly at an anatomically distant site. Persons receiving RIG for recalled vaccine administered as part of a preexposure vaccination series should have as much of the dose as is anatomically feasible infiltrated at the site(s) where recalled vaccine was administered, and the rest should be administered intramuscularly at an anatomically distant site. RIG should never be administered in the same syringe as vaccine, or into the same anatomical site used for concomitant vaccination. Because RIG might partially suppress active production of antibody, no more than the recommended dose should be administered.

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